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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,869	10/12/2005	Anders Lehmann	1103326-0946	3025

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PATENT DEPARTMENT
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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
08/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,869	LEHMANN ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-28* is/are pending in the application.

4a) Of the above claim(s) *19-23,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15, 17, 18,24,25 and 28* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/4/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

In response to the Decision from the Pre-Appeal Brief Review of January 15, 2009, the rejection of record under 35 U.S.C. 112, second paragraph, and the rejection under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, are withdrawn. Further, the search and examination for the present application has been extended beyond the elected compound, 2-methyl-6-(phenylethynyl)-pyridine (MPEP), to include the species 3-[3-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl]-5-(methoxymethyl)benzonitrile and 3-fluoro-5-[3-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl]benzonitrile.

Claims 15-28 are pending. In response to the Restriction Requirement set forth in the Office Action of May 16, 2007, Applicants elected Group I, drawn to methods for inhibiting transient lower esophageal sphincter relaxations (TLESRs), for the treatment of GERD, for the prevention of reflux, and for the treatment or prevention of regurgitation, comprising administering a metabotropic glutamate receptor 5 antagonist. Applicants reiterate their traversal and urge the present invention is directed to the use of mGluR5 antagonists for the inhibition of transient lower esophageal sphincter relaxations and for the treatment of GERD. In Applicants' view, "any burden on the Examiner to perform a prior art search of the genus of mGluR5 antagonists is outweighed by Applicants' expense and the public detriment stemming from protracted examination based on an arbitrary sorting of species..."

Applicants' traversal has been repeatedly addressed in previous Office Actions. The prior art teaches metabotropic glutamate receptors have ubiquitous effects. In addition to mediating glutamatergic synaptic transmission by acting at ionotropic

receptors, glutamate also activates a family of G-protein-coupled receptors that modulate neuronal excitability and synaptic transmission. See Martin et al., Neurogastroenterology & Motility Conference (2001). Further, in view of the sensitivity or specificity of said receptors, and the various functionalities encompassed among those compounds that are deemed to be metabotropic glutamate receptor 5 (mGluR5) antagonists, an undue search burden is presented to the Examiner.

The Restriction Requirement and Election of Species Requirement are still deemed proper and are adhered to. The **FINALITY** of the Requirements is reiterated.

The subject matter under consideration remains those methods of treatment drawn to inhibiting transient lower esophageal sphincter relaxations (TLESRs), treating GERD, inhibiting reflux of gastric juice, and treating regurgitation of gastric juice comprising administering one of the three metabotropic glutamate receptor 5 antagonists that are disclosed in specification, 2-methyl-6-(phenylethynyl)-pyridine (MPEP), 3-[3-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl]-5-(methoxymethyl)benzonitrile or 3-fluoro-5-[3-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl]benzonitrile, claims 15-18, 24, 25 and 28.

Those methods drawn to other treatments, as well as the administration of metabotropic glutamate receptor 5 antagonists other than the 3 species recited *supra*, and claims 19-23, 26 and 27, remain withdrawn from consideration by the Examiner, as drawn to non-elected inventions, 37 CFR 1.142(b).

An Information Disclosure Statement filed May 4, 2009 is acknowledged and has been reviewed to the extent each reference is a proper citation on a US patent. All references have been considered.

The following objection and rejections set forth below constitute the only objection and rejections that are presently applied to the instant claims.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claims 17, 18, 24, 25 and 28 remained rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention, in the last Office Action. None of the present claims recite "prevention" of reflux or regurgitation. However, the specification on page 3, line 5, and page 4, lines, 1-3, indicates methods drawn to prevention of regurgitation (claim 18) and to prevention of reflux of gastric juice (claim 17) are encompassed. The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation.

While it is well established that TLESRs are a dominant characteristic of GERD, they are not the sole pathophysiologic mechanism through which reflux disease occurs. The term "prevent" is an absolute definition that means to stop from occurring and thus

requires a higher standard for enablement than does "therapeutic" or "treat". Applicants have failed to provide guidance as to which particular compound would be preferred for preventing reflux or preventing regurgitation comprising administering a metabotropic glutamate receptor 5 antagonist. The characterization of a particular compound as a metabotropic glutamate receptor 5 antagonist does not presage efficacy for preventing reflux or preventing regurgitation in view of the diverse functionalities of the compounds of the instant claims. The prior art does not recognize metabotropic glutamate receptor 5 antagonist for use in the claimed preventative methods of use.

The rejection of record of claims 17, 18, 24, 25 and 28 under 35 U.S.C. 112, first paragraph, is maintained because the high degree of unpredictability for the prevention of reflux and regurgitation. The lack of guidance provided by the specification would have required undue experimentation. In order to obviate this rejection, Applicants may consider deleting embodiments in the specification that are drawn to a prevention modality.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 17, 18, 24, 25 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Independent claims 15, 17 and 18 are now drawn, respectively, to methods of inhibiting transient lower esophageal sphincter relaxations (TLESRs), to methods for

inhibiting reflux of gastric juice and to methods for treating regurgitation of gastric juice comprising administering a metabotropic glutamate receptor 5 antagonist. Passages from The Merck Index were provided to show various and unrelated etiologic factors may cause or be the result of TLESRs. Even though GERD may be the result of incompetence of the lower esophageal sphincter, variations in intrinsic sphincter pressure, the presence or absence of an inflammatory process, the angle of the cardio-esophageal junction, the action of the diaphragm, the effect of gravity, the volume of gastric contents, local mucosal protective functions and the general health status of the patient must be considered. A clear nexus between the preamble of each claim and a patient suffering from gastroesophageal reflux disease is absent. While the Tables on page 11 demonstrate a percent inhibition of TLESRs in an animal model following the administration of MPEP or 3-fluoro-5-[3-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl]benzonitrile, reflux may or may not be of a gastroesophageal origin. Regurgitation may or may not be limited to a pediatric population. The prior art recognized transient lower esophageal sphincter relaxations may be caused by unrelated, or etiologically distinct, factors.

This rejection may be overcome by establishing in the preamble of claims 15, 17 and 18 that those patients in need of inhibiting TLESRs, those in need of Inhibiting reflux of gastric juice and those in need of treatment of regurgitation of gastric juice, are suffering from GERD.

Favorable consideration would be given to a claim drawn to the treatment of GERD comprising administering 2-methyl-6-(phenylethynyl)-pyridine (MPEP), 3-[3-(5-

fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl]-5-(methoxymethyl)benzonitrile or 3-fluoro-5-[3-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl]benzonitrile.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 13, 2009

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614